

What is claimed is:

1. A method of imaging cells comprising a glycoprotein hormone receptor, said method comprising administering to a subject a modified glycoprotein hormone, said modified glycoprotein hormone having at least one mutation that increases the hormone activity relative to the wild type glycoprotein hormone and detecting said modified glycoprotein hormone.
2. The method of Claim 1 wherein the modified glycoprotein hormone is a modified thyroid stimulating hormone (TSH).
3. The method of Claim 1 wherein the modified glycoprotein hormone is a modified follicle-stimulating hormone (FSH).
4. The method of Claim 1 wherein the modified glycoprotein hormone is a lutenizing hormone (LH).
5. The method of Claim 1 wherein the modified glycoprotein hormone is chorionic gonadotropin (CG).
6. The method of Claim 2 wherein the modified TSH differs from the wild type TSH in that the modified TSH  $\alpha$ -subunit comprises at least one basic amino acid at positions selected from the group consisting of 11, 13, 14, 16, 17, 20 and 22.
7. The method of Claim 6 wherein the modified TSH comprises at least one basic amino acid at position 1, 6, 17, 58, 63, 66, 69 and 81 of the  $\beta$ -subunit.
8. The method of Claim 6 wherein the modified TSH comprises at least three basic amino acids at positions 11, 13, 14, 16, 17, 20 or 22 of the  $\alpha$ -subunit.
9. The method of Claim 6, 7 or 8 wherein the basic amino acids are lysine or arginine.
10. The method of Claim 1 wherein the cells comprising a glycoprotein hormone receptor are cancerous cells or cells indicative of an autoimmune disorder.
11. The method of Claim 1 wherein detecting increased levels of said modified glycoprotein hormone in said subject indicates the presence of cancerous cells or an autoimmune disorder.

12. The method of Claim 11 wherein the cancerous cells are thyroid carcinoma cells.
13. The method of Claim 11 wherein the cancerous cells are selected from the group consisting of ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, lung cancer, teratomas, breast cancer, testicular cancer or pituitary tumor.
14. The method of Claim 11 wherein the autoimmune disorder is Graves' disease or Hashimoto's disorder.
15. The method of Claim 1 wherein said modified glycoprotein hormone is labeled.
16. The method of Claim 15 wherein the label is a radiopaque label, radioisotope label, fluorescence label or paramagnetic label.
17. The method of Claim 16 wherein the radiopaque label is an ionic or nonionic agent.
18. The method of Claim 17 wherein the ionic agent is selected from the group consisting of diaztrizoate meglumine 30%, diaztrizoate meglumine 60%, diaztrizoate meglumine 66%, diaztrizoate sodium 10%, diaztrizoate sodium 50%, iothalamate meglumine 30%, iothalamate meglumine 43%, iothalamate meglumine 60%, ioxaglate meglumine 39.3%, iothalamate sodium 19.6% or combinations thereof.
19. The method of Claim 17 wherein the nonionic agent is selected from the group consisting of gadodiamide, gadoteridol, gadoversetamide, iodixanol 270, iodixanol 320, iohexol 140, iohexol 180, iohexol 240, iohexol 300, iohexol 350, iopamidol 41%, iopamidol 51%, iopamidol 61%, iopamidol 76%, iopromide 150, iopromide 240, iopromide 300, iopromide 370, ioversol 34%, ioversol 51%, ioversol 64%, ioversol 68%, ioversol 74% or combinations thereof.
20. The method of Claim 16 wherein the radioisotope label is  $I^{131}$  or  $Tc^{99m}$ .

21. The method of Claim 16 wherein the paramagnetic label is gadodiamide, gadoteridol, gadoversetamide, ferumoxides, gadopentetate dimeglumine, mangafodipir trisodium, or combinations thereof.
22. The method of Claim 1 further comprising administration of protirelin, thyrotropin alpha, gonadorelin or combinations thereof.
23. The method of Claim 15 wherein the labeled modified glycoprotein hormone is detected by a method selected from group consisting of magnetic resonance imaging, computed tomography imaging, nuclear medicine imaging, X-ray, mammography, radionuclide imaging or combinations thereof.
24. The method of Claim 15 wherein detecting an amount of said labeled modified glycoprotein hormone in said subject indicates the presence of cancerous cells or an autoimmune disorder.
25. The method of Claim 24 wherein the cancer is thyroid cancer.
26. The method of Claim 24 wherein the cancer is selected from the group consisting of ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, lung cancer, teratomas, breast cancer, testicular cancer or pituitary tumor.
27. The method of Claim 24 wherein the autoimmune disorder is Graves' disease or Hashimoto's disorder.
28. A method of delivering an agent to a cell expressing a glycoprotein receptor to a subject in need thereof, said method comprising administering to said subject an agent coupled to a modified glycoprotein hormone having at least one mutation that increases the hormone activity relative to the wild type glycoprotein hormone.
29. The method of Claim 28 wherein the modified glycoprotein hormone is a modified TSH.
30. The method of Claim 28 wherein the modified glycoprotein hormone is a modified FSH.
31. The method of Claim 28 wherein the modified glycoprotein hormone is a modified LH.

32. The method of Claim 28 wherein the modified glycoprotein hormone is modified CG.
33. The method of Claim 29, wherein the modified TSH differs from the wild type TSH in that the modified TSH  $\alpha$ -subunit comprises at least one basic amino acid at positions selected from the group consisting of 11, 13, 14, 16, 17, 20 and 22.
34. The method of Claim 29 wherein the modified TSH comprises at least one basic amino acid at position 1, 6, 17, 58, 63, 66, 69 and 81 of the  $\beta$ -subunit.
35. The method of Claim 29 wherein the modified TSH comprises at least three basic amino acids at positions 11, 13, 14, 16, 17, 20 or 22 of the  $\alpha$ -subunit.
36. The method of Claim 33, 34 or 35 wherein the basic amino acids are lysine or arginine.
37. The method of Claim 28 wherein said agent is selected from the group consisting of cytoprotective compounds, antibodies, drugs, sensitizers, biological response modifiers, radionuclides, toxins, viruses or combinations thereof.
38. The method of Claim 37 wherein the agent is a drug selected from the group consisting of natural or synthetic estrogens, estrogen receptor modulators, progestins, androgens, ovulation stimulants, gonadotropin-releasing hormones, androgen inhibitors, bisphosphonates, glucocorticoids, thyroid hormones, antithyroid agents, alkylating agents, antimetabolites, antimitotic agents, epipodophyllotoxins, antineoplastic antibiotics, antineoplastic hormones, platinum coordination complex agents, anthracenediones, substituted ureas, methylhydrazine derivatives, DNA topoisomerase inhibitors, retinoids, or combinations thereof.
39. The method of Claim 38 wherein the drug is selected from the group consisting of clomiphene, finasteride, propylthiouracil, methimazole, bleomycin, vincristine, vinblastine, cisplatin, mitomycin, ifosfamide, cyclophosphamide, doxorubicin, paclitaxel, fluorouracil, carboplatin, epirubicin, altretamine, vinorelbine, mitoxantrone, bromocriptine, prednisone, porfimer, mitotane or combinations thereof.

40. The method of Claim 38 wherein the sensitizer is selected from the group consisting of metronidazole, misonidazole, verapamil, diltiazem or combinations thereof.
41. The method of Claim 37 wherein the agent is a biological response modifier selected from the group consisting of interferon- $\alpha$ , interferon- $\beta$ , interferon- $\gamma$ , tumor necrosis factor, lymphotoxin, interleukin-1, interleukin-2, interleukin-3, interleukin-4, interleukin-5, interleukin-6, p53 or combinations thereof.
42. The method of Claim 37 wherein the agent is a monoclonal antibody, polyclonal antibody or combination thereof.
43. The method of Claim 37 wherein the agent is a cell signal transduction pathway modifier.
44. The method of Claim 43 wherein the agent is selected from the group consisting of forskolin, staurosporine, phorbol esters, non-steroidal antiinflammatory drugs, steroids, or combinations thereof.
45. The method of Claim 37 wherein the agent is a cytoprotective compound.
46. The method of Claim 43 wherein the cytoprotective compound is mesna or leucovorin.
47. The method of Claim 37 wherein the radionuclide is selected from the group consisting of  $^{131}\text{I}$ ,  $^{132}\text{I}$ ,  $^{32}\text{P}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{203}\text{Pb}$ ,  $^{212}\text{Pb}$ ,  $^{212}\text{Bi}$ ,  $^{109}\text{Pd}$ ,  $^{64}\text{Cu}$ ,  $^{67}\text{Cu}$ ,  $^{211}\text{At}$ ,  $^{97}\text{Ru}$ ,  $^{105}\text{Rh}$ ,  $^{198}\text{Au}$  and  $^{199}\text{Au}$ .
48. The method of Claim 37 wherein the toxin is ricin, abrin, diphtheria toxin, *Pseudomonas* exotoxin A, ribosomal inactivating proteins, and mycotoxins.
49. The method of Claim 37 wherein the viruses are selected from the group consisting of adenovirus, retrovirus or combinations or fragments thereof.
50. The method of Claim 28 wherein the subject has or is suspected of having a disorder selected from the group consisting of thyroid cancer, Graves' disease, Hashimoto's disorder, ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, lung cancer, teratomas, breast cancer, testicular cancer or pituitary tumor.
51. A method for the detection of an analyte that interferes with the binding of a modified glycoprotein hormone to a glycoprotein receptor in a biological

- sample, said method comprising (i) contacting the sample, with a modified glycoprotein hormone, said modified glycoprotein hormone having at least one mutation that increases the hormone activity relative to the wild type glycoprotein hormone and (ii) detecting a signal wherein the presence or amount of the signal detected indicates the presence or absence of an analyte that interferes with the binding of a modified glycoprotein hormone to a glycoprotein receptor.
52. The method of Claim 51 wherein the signal is the presence or amount of the modified glycoprotein hormone bound with the glycoprotein receptor in the biological sample.
53. The method of Claim 51 wherein the signal is the presence or amount of cAMP in the biological sample.
54. The method of Claim 51 wherein the signal is the presence or amount of steroids in the biological sample.
55. The method of Claim 54 wherein the signal is the presence or amount of progesterone in the biological sample.
56. The method of Claim 51 wherein the signal is the presence or amount of inositol trisphosphate or other component of inositol phosphate pathway.
57. The method of Claim 51 wherein the signal is the presence or amount of intracellular calcium, activity of calcium-dependent kinases or a combination thereof.
58. The method of Claim 51 wherein the signal is the presence or activity of protein kinase B (PKB) or serum/glucocorticoid-induced kinase (Sgk).
59. The method of Claim 51 wherein the modified glycoprotein hormone is a modified TSH.
60. The method of Claim 51 wherein the modified glycoprotein hormone is a modified FSH.
61. The method of Claim 51 wherein the modified glycoprotein hormone is a modified LH.

62. The method of Claim 51 wherein the modified glycoprotein hormone is modified CG.
63. The method of Claim 59 wherein the modified TSH comprises at least one basic amino acid at a position selected from the group consisting of 11, 13, 14, 16, 17, 20 and 22 of the  $\alpha$ -subunit.
64. The method of Claim 59 wherein the modified TSH comprises at least one basic amino acid at a position selected from the group consisting of 1, 6, 17, 58, 63, 66, 69 and 81 of the  $\beta$ -subunit.
65. The method of Claim 60 wherein the modified FSH comprises at least one basic amino acid at a position selected from the group consisting of 13, 14, 16, 17, 20, 21, 22, 66, 68, 73, 74 and 81 of the  $\alpha$ -subunit.
66. The method of Claim 60 wherein the modified FSH comprises at least one basic amino acid at a position selected from the group consisting of 2, 4, 14, 63, 64, 67 and 69 of the  $\beta$ -subunit.
67. The method of Claim 63, 64, 65 or 66 wherein the basic amino acids are lysine or arginine.
68. The method of Claim 51 wherein the analyte is an antibody to a glycoprotein receptor.
69. The method of Claim 51 wherein the analyte is an antibody to a glycoprotein hormone receptor extracellular domain.
70. The method of Claim 51 wherein the analyte is wild type glycoprotein hormone.
71. The method of Claim 51 wherein the glycoprotein receptor is selected from the group consisting of receptors for TSH, FSH, LH, CG or combinations thereof.
72. The method of Claim 51 wherein said modified glycoprotein hormone is labeled.
73. The method of Claim 51 wherein the biological sample comprises whole cells.

74. The method of Claim 51 wherein the biological sample comprises cell membranes.
75. The method of Claim 51 wherein the detection of the signal indicates that the subject from whom the biological sample was acquired is suffering from a disorder selected from the group consisting of thyroid cancer, Graves' disease, Hashimoto's disorder, ovarian cancer, uterine cancer, endometrial cancer, lung cancer, teratomas, breast cancer, testicular cancer, pituitary tumor, ovulatory dysfunction, luteal phase defect, unexplained infertility, male factor infertility, time-limited conception or spontaneous abortion.